Remarks

Applicant greatly appreciates the Examiner's very careful review of the application, which is evident from her identification of multiple typographical errors and claim syntax errors. Applicant's new counsel will endeavor to write clearly and accurately, so as to avoid burdening the Examiner with such proof-reading.

Applicant submits the following remarks in support of the patentability of the pending claims, which remarks are focused on the independent claims, since if these are found patentable, so will their respective dependent claims be patentable without further consideration.

The Concerns Regarding Drawings, Title and Abstract

Applicant acknowledges paragraphs 3-5 on page 2 of the Office action, wherein the Examiner objects or expresses concern with respect to the drawings, and the title and abstract of the application not being sufficiently descriptive. In that regard, Applicant respectfully requests that these changes be held in abeyance until such time as one or more claims may be found allowable. While Applicant recognizes that these changes would be beneficial, the added time would be helpful to new counsel, given that this response is filed on the last day available to do so.

The Objections To The Claims

All of the informalities noted by the Examiner have been corrected by appropriate claim amendments.

The Claims Meet The Requirements Of Section 112

All of the Examiner's concerns under Section 112 have been corrected by appropriate claim amendments as well. Claims 10 and 37 have been cancelled.

The Claims Are Novel Over The Cited References

The Examiner rejected claim 37 under 35 USC 102 as anticipated by Daniell (WO99/10513). Claim 37 has now been cancelled.

The Examiner also rejected independent claims 1, 29, 34, 36 and 37 under 35 USC 102 as anticipated by Daniell et al. (WO01/64024). In that regard, Applicant points out that the Examiner has recognized that WO01/64024 does not disclose BADH as the selectable marker (Office action, page 6, under paragraph 14). Applicant has amended these claims to recite an antibiotic-free selectable marker, which BADH is. The cited reference only discloses antibiotic resistance genes as selectable markers, with the aadA gene for spectinomycin resistance as the only given example (see paragraph 030).

Accordingly, Applicant is hopeful that these claims now clearly distinguish over the cited reference and respectfully requests that the anticipation rejections be withdrawn.

The Claims Are Nonobvious Over Daniell et al. and Rathinasabapathi et al.

Independent claims 1, 29, 34, 36 and 37 stand rejected as obvious under 35 USC 103(a) over the combined references of Daniell et al. (WO01/64024) and Rathinasabapathi et al. (1994, *Planta* 193:155-162). Applicant respectfully disagrees for the following reasons.

As noted above, the reference by Daniell et al. does not disclose BADH or an antibiotic-free selectable marker. All these claims have been clarified to recite same.

The reference by Rathinasabapathi et al. describes transformation of tobacco plants but the transformation occurs in the nuclear genome, not in a plastid genome. The Examiner contends that Rathinasabapathi et al. suggest the use of betaine aldehyde as a selectable marker and recognizes that the reference teaches a nuclear transformation but she asserts that it would have been a design choice to transform a plastid genome instead of the nuclear genome. The Examiner relies on the statement by Rathinasabapathi et al. that the protein is targeted to the chloroplasts. Applicant disagrees and points to the following teachings of Rathinasabapathi et al.

First, notwithstanding the statement in the reference that the protein is targeted to the chloroplasts, Rathinasabapathi et al. admit that "our data do not exclude the possibility that BADH is located in the chloroplast intermembrane space." See page 158, left hand column at end of first paragraph. Applicant submits that their data also do not indicate whether the protein may be along the inside of the envelope or the outside of the envelope, only that it is associated with the envelope.

Therefore, Rathinasabapathi et al. strongly suspect that the protein is associated with the chloroplasts, but they do not know its specific location. The protein could be associated anywhere on the chloroplast envelope, which is known to consist of an inner and an outer phospholipid membrane with the intermembrane space therebetween. If the protein were to be associated along the outer surface of the chloroplast envelope, its substrate (betaine aldehyde) would likely not require transport into the chloroplast stroma.

Keeping that in mind, Applicant points to the next unfavorable admission by Rathinasabapathi et al. On page 161, in the left hand column, last paragraph, they

state: "Although transgenic plants metabolize betaine aldehyde at rates sufficient to confer resistance to this compound, *their growth is still retarded compared to controls*." Emphasis added. We should remember that Rathinasabapathi et al. teach nuclear transformation and that their enzyme may be localized along the outer surface of the chloroplast envelope. Consequently, Applicant suggests that this retarded, stunted growth of the transgenic plants admitted by Rathinasabapathi et al. is due to the adverse interaction of the betaine aldehyde with the cytoplasm at the surface of the chloroplast envelope. Rathinasabapathi et al. did not recognize the solution to this problem and were, thus, limited to reporting their somewhat unsatisfactory results.

Applicant respectfully suggests that the solution to the problem encountered by Rathinasabapathi et al., stunted growth in their nuclear transformed plants, is provided in the presently claimed invention. Accordingly, there is nothing taught in either cited reference that would have led those of ordinary skill to the solution disclosed by Applicant.

If the Examiner is relying on her own expertise to support the assertion that chloroplast transformation would have been a mere design choice over the nuclear transformation taught by Rathinasabapathi et al., Applicant respectfully requests that she introduce such evidence into the record in an affidavit or declaration to that effect.

Applicant believes that those of ordinary skill in the art would not have been able to combine the Daniell et al. reference with that by Rathinasabapathi et al. to arrive at the presently claimed invention. Neither do the combined references, if they were able to be combined, produce all the features of the claimed invention. For those reasons, Applicant respectfully requests that the obviousness rejection of these claims, based on the references of record, be withdrawn.

The Claims Are Nonobvious Over Daniell and Meagher et al.

The Examiner has also rejected independent claims 1, 34 and 36 as obvious and unpatentable over Daniell (WO 99/10513) in view of Meagher et al. (US 5,965,796). Applicant respectfully disagrees, for the following reasons.

As noted above, the Examiner has recognized that the reference by Daniell does not disclose merA or merB in those vectors. The cited reference by Meagher et al., however, does describe the merA and merB genes but it does not describe inserting those genes into a plant by plastid transformation. The Examiner, nevertheless, contends that "one of ordinary skill in the art would have been motivated to do so because expression as an operon in the plastid would allow production of stoichiometric amounts of the two enzymes in the pathway."

Applicant notes that the Examiner has identified one of the great advantages of the presently claimed invention, but disagrees that such would have been obvious to one of ordinary skill in the art in view of the cited references. In fact, the cited reference by Meagher et al. is a continuation-in-part of a parent application which issued on September 16, 1997, as US Patent No. 5,668,294, titled Metal Resistance Sequences And Transgenic Plants. Clearly, as indicated by its title, this parent application to the cited reference also involved transgenic plants and metal resistance, particularly mercury. As an inventor recipient of a US Patent, Meagher is not of ordinary skill but is a person of extraordinary skill in the art. Yet, when Meagher et al. filed the application which resulted in the cited reference, a continuation-in-part of US Patent No. 5,668,294, they did not appreciate the advantage noted by the Examiner, that expression of the two enzymes required for mercury remediation as an operon in the plastid genome would produce stoichiometric amounts of the two enzymes in the pathway.

Therefore, contrary to the Examiner's contention, these facts indicate that even one of extraordinary skill in the art did not recognize the advantages of the presently claimed invention. Chloroplast transformation by use of a gene gun has been known since at least about 1993 (Daniell, H. (1993) *Methods in Enzymology*, 217:536-556; see cited reference WO 99/10513, at page 4, line 5). Yet, even with this information available, Meagher et al., people of extraordinary skill in the art who filed patent applications in 1995 (parent patent to the cited reference) and 1997 (the cited reference), failed to recognize the possibility of the present invention not once, but twice. Applicant believes that these facts provide strong evidence that the contention that the presently claimed invention would have been obvious is incorrect.

For those reasons, Applicant respectfully requests that the obviousness rejections of these claims based on the combined references of Daniell, in view of Meagher et a., be withdrawn.

Conclusion

For the reasons set forth above, Applicant believes the pending claims are patentable over the cited art and respectfully requests such action from the Examiner. Applicant acknowledges that there would still be drawing corrections required, as well as amendments needed to the title and to the abstract.

If further prosecution may be aided by a conference, Applicant respectfully requests that counsel be contacted by telephone at the Examiner's convenience.

Respectfully submitted,

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